made concerning reducing the growth of unwanted hair. See also, for example, Ahluwalia et al. (AA on Form 1449 filed June 13. 1995); Shander et al. (AE); Shander et al. (AF); Ahluwalia et al. (BA); Ahluwalia (BB); Breuer et al. (BC); Shander (BD); Shander et al. (DI); Ahluwalia et al. (DJ); Ahluwalia (DK); and Ahluwalia et al. (AA on Form 1449 filed on February 13, 1997).

The present invention relates to angiogenesis, which is the development of new blood vessels. There are at least seven pathways that are known to be involved in angiogenesis. These pathways, and the various established ways to interfere with the pathways in order to suppress angiogenesis, are discussed extensively by applicants in the Background and Summary of the Invention sections of the application.

Generally, applicants conceived that if they could suppress angiogenesis in an area of skin, they could cause a reduction in the amount of hair growth from that area of skin. Applicants wanted to test their concept and accordingly searched the literature to find chemicals that are known to be suppressors of angiogenesis. They selected 19 non-steroidal compounds for evaluation. The selected non-steroidal compounds were dissolved in the appropriate vehicle, and applied topically as described on pages 9-12 of the specification. Every compound that applicants tested as part of this project caused a reduction in hair growth. The results of the testing are provided in Table 1 in the application; Table 1 is reproduced below for the convenience of the Examiner:

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TABLE

Compound	Dose	Vehicle*	pH	Hair Mass Treated(mg)	Hair Mass Control(mg)	%Inhibition
bathocuproine	10%	A	7.0	0.41 ± .06	2.23 ± .20	81 ± 3
p-nitrocatechol sulfate	10%	A	9.0	0.58 ± .08	2.39 ± .21	74 ± 5
aurintricarboxylic acid	10%	A	4.0	0.92 ± .08	2.70 ± .29	66 ± 2
mycophenolic acid	10%	D	4.0	0.60 ± .13	1.85 ± .19	65 ± 8
nafoxidine	10%	A	5.0	0.76 ± .19	1.70 ± .14	59 ± 8
tamoxifen	10%	A	4.5	0.72 ± .17	1.65 ± .24	56 ± 12
catechin	10%	A	4.5	0.56 ± .12	1.31 ± .12	56 ± 8
quinacrine	10%	A	6.0	1.27 ± .23	2.50 ± .40	50 ± 8
O-p-nitrohydroxylamine	10%	A	4.0	0.94 ± .17	1.82 ± .21	50 ± 5
diethylenetriamine pentaacetic acid	7.5%	B	4.0	1.31 ± .22	2.44 ± .28	49 ± 8
cimetidine	10%	A	8.0	0.95 ± .14	1.85 ± .23	46 ± 7
lisinopril	7.5%	A	5.0	0.79 ± .14	1.50 ± .23	44 ± 10
piracetam	10%	A	6.0	0.89 ± .18	1.44 ± .22	38 ± 10
enalapril	10%	C	5.0	1.25 ± .16	2.06 ± .11	38 ± 9
pentosan polysulfate	10%	A	6.5	1.07 ± .16	1.57 ± .12	33 ± 7
terfenadine	5%	B	8.0	1.50 ± .26	2.18 ± .26	32 ± 8
tripelennamine	10%	A	6.5	1.20 ± .23	1.80 ± .23	30 ± 9
chlorfeniramine	10%	A	6.0	0.92 ± .16	1.40 ± .21	29 ± 12
tranexamic acid	10%	A	5.5	1.47 ± .13	2.01 ± .15	21 ± 12

*vehicle A = 68% H_2O; 16% ethanol; 5% propylene glycol; 4% benzyl alcohol; 2% propylene carbonate

B = 80% H_2O; 10% dipropylene glycol; 10% ethanol

C = 80% ethanol; 17.5% H_2O; 2% propylene glycol dipelargonate; 0.5% propylene glycol

D = 70% ethanol; 30% dimethylsulfoxamine

The non-steroidal compounds tested by applicants suppress angiogenesis in a variety of ways, as explained in the specification. For example, catechin is an inhibitor of the enzyme sulfotransferase; pentosan polysulfate is a heparin binding antagonist; cimetidine is a histamine receptor antagonist; and piracetam is an inhibitor of prostogladin synthetase.

Claim 1 is a method claim directed to the generic invention. Claim 1 requires (1) selecting an area of skin from which reduced hair growth is desired, and (2) applying a non-steroidal suppressor of angiogenesis to that area of skin in an amount effective to cause a reduction in hair growth.

Thus, applicants have made a significant and broad contribution to the art, have conducted substantial testing to demonstrate their contribution, and have submitted a claim (claim 1) that is commensurate in scope with their contribution.

35 U.S.C. §112, ¶2 Rejection

Claims 1, 8, 21-29, 42, and 43 were rejected under 35 U.S.C. §112, ¶2 because applicants use the words "reducing" hair growth in the claims. But what is meant by reducing hair growth is described expressly in the specification (see page 9, lines 14-18).

> Reduction in hair growth is demonstrated when the frequency of hair removal is reduced, or the subject perceives less hair on the treated site, or quantitatively, when the weight of hair removed by shaving (i.e., hair mass) is reduced.

A person of ordinary skill in the art would understand what is meant by this explanation. Indeed, "reducing" hair growth has been used by applicants in claims previously, and consistently has been accepted by the Patent and Trademark Office. For example, in Ahluwalia et al. (AA on Form 1449 filed on June 13, 1995), claim 1 is directed to reducing hair growth using, e.g., pantothenic acid. As the inventors explained in the specification (col. 3, lines 23-27):

> Reduction of hair growth is demonstrated when the frequency of hair removal is reduced, or the subject perceives less hair on the treated site, or quantitatively, when the weight of hair removed by shaving (i.e., hair mass is reduced).

Similarly, in Ahluwalia et al., (DJ), now U.S. Patent No. 5,455,234, copy enclosed, claim 1 relates to reducing hair growth using an inhibitor of a cysteine pathway enzyme. As the inventors explained in the specification (col. 2, line 66 to col. 3, line 3):

> Reduction in hair growth is demonstrated when the frequency or hair removal is reduced, or the subject perceives less hair on the treated site, or quantitatively, when the weight of hair removed by shaving (i.e., hair mass) is reduced.

Likewise, in Ahluwalia et al. (AA in Form 1449 filed on February 13, 1997), the claims are directed to reduced hair growth using an inhibitor of kinase C. As the inventors explained in their specification (col. 2, lines 48-53):

> Reduction in hair growth is demonstrated when the frequency of hair removal (shaving, tweezing, depilatory use, waxing) is reduced, or the subject perceives less hair on the treated site, or quantitatively, when the

> weight of hair removed by shaving (i.e., hair mass is reduced.

According to 35 U.S.C. § 112, ¶ 2,

> [t]he specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which applicant regards as his invention.

As the Court explained in In re Wakefield, 164 U.S.P.Q. 636, 641 (C.C.P.A. 1970):

> The meaning of this provision is simply that an applicant is required to set definite boundaries on the patent protection sought.

The purpose of the requirements of 35 U.S.C. § 112, ¶ 2 is

> to provide those who would endeavor, in future enterprise, to approach the area circumscribed by the claims of a patent, with the adequate notice demanded by due process of law, so that they may more readily and accurately determine the boundaries of protection involved and evaluate the possibility of infringement and dominance.

In re Hammack, 166 U.S.P.Q. 204, 208 (C.C.P.A. 1970).

These requirements clearly are met by the language "reducing" hair growth in claim 1. The specification provides a clear explanation of what applicants mean by this language, and as demonstrated above the meaning is well understood in the art. A person of ordinary skill in the art would have no difficulty perceiving whether hair growth has been reduced. Should the Examiner decide to maintain the rejection, applicants request that the Examiner provide evidence to support his position that a person skilled in the art would not understand what is meant by reducing hair growth, so that applicants can address this evidence.

Finally, the Examiner apparently believes that "reducing" is "relative" and therefore claims including the language are invalid. Amgen Inc. v. Chugai Pharmaceutical Co., 18 U.S.P.Q. 2d 1016 (Fed. Cir. 1991) is cited for support. But Amgen concerned the claim limitation "about 160,000", and the court found the claim invalid under 35 U.S.C. § 112, ¶ 2 because the inventor did not explain the scope of "about 160,000" in the specification. Id. at 1030-31. This fact scenario has no bearing on applicants' use of "reducing", which is explained clearly in the specification.

35 U.S.C. § 112, ¶ 1 Rejection

1. **The law**

As explained by the Board of Appeals in Ex parte Forman, 230 U.S.P.Q. 546, 547 (1986), 35 U.S.C. §112, ¶ 1 requires applicants to provide a sufficient disclosure

> to enable one having ordinary skill in the relevant field to practice the invention claimed therein without the exercise of undue experimentation.

The Board went on to explain the factors that are considered in deciding when experimentation becomes "undue" (id.):

> The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art: Ansul Co. v. Uniroyal, Inc. [169 U.S.P.Q. 759, 762 (2d Cir. 1971)].
>
> * * *
>
> The factors to be considered have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence

> of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. In re Rainer, 52 CCPA 1593, 347 F.2d 574, 146 USPQ 218 1965); In re Colianni, supra.

A person skilled in the art, reading applicants specification, would be able to practice the claimed invention -- reducing hair growth by topical application of non-steroidal suppressors of angiogenesis -- without undue experimentation. Therefore, the applicants have met the requirements of 35 U.S.C. § 112, ¶ 1.

Applicants will apply each of the factors mentioned in Forman to the current facts, and explain why the facts demonstrate that the claimed invention can be practiced without undue experimentation. Applicants will begin with a key factor, the nature of the invention.

a. **Nature of the invention**

What is meant by "the nature of the invention" was discussed in the Ansul decision cited by the Board in Forman. In Ansul the Court explained that inventors who discover "a new use for existing composition" are entitled to broad, generic claims even if the inventors have not disclosed every potential embodiment of the invention (see 169 U.S.P.Q. at 762).

What this means in the context of the present invention is that applicants are not required to disclose and test every non-steroidal suppressor of angiogenesis in order to be entitled to a generic patent. The invention is not new non-steroidal suppressors of angiogenesis. Rather, like in Ansul, applicants

discovered a new use (reducing hair growth) for compounds (non-steroidal suppressors of angiogenesis) that are well known. The Court addressed this very issue in In re Fuetterer, 138 U.S.P.Q. 217, 223 (1963):

> Appellant's invention is the combination claimed and not the discovery that certain inorganic salts have colloid suspending properties....The invention description clearly indicates that any inorganic salt which has such properties is usable in his combination. If others in the future discover what inorganic salts additional to those enumerated do have such properties, it is clear appellant will have no control over them per se, and equally clear his claims should not be so restricted that they can be avoided merely by using some inorganic salt not named by appellant in his disclosure. The only "undue burden" which is apparent to us in the instant case is that which the Patent Office has attempted to place on the appellant.

b. Quantity of experimentation necessary

A person skilled in the art would have to conduct virtually no experimentation to practice the invention broadly. Over 40 non-steroidal suppressors of angiogenesis are identified in applicant's specification, along with suitable vehicles and protocols. A person skilled in the art, looking to find additional non-steroidal suppressors, simply could do what applicants did -- search the literature.

Moreover, to the extent there is doubt that a particular suppressor that is not among those tested by applicants would reduce hair growth, the specification provides a very straight-forward test that can be used to identify easily those suppressors (if any) that do not work to reduce hair

growth. Cf. In re Wands, 8 U.S.P.Q.2d 1400, 1404-06 (Fed. Cir. 1988) (finding no undue experimentation where specification provided screening test).

The lack of experimentation necessary to practice the invention further brings out why applicants are entitled to broad protection. The Court in Ansul described how easy it is under these circumstances for others to appropriate an inventor's contribution (169 U.S.P.Q. at 762, quoting district court):

> With astonishing rapidity [the infringers] used the new discovery and teachings in routine experiments, featuring routine screening techniques, to develop practical uses for the product. None of this would have occurred, of course, if it had not been for Uniroyal's disclosure of the basic secret with sufficient information for researchers to use the compound in their regular sampling procedures.

c. The presence or absence of working examples

Applicants have not only provided a working example, they have provided 19 working examples (see Table 1, which was reproduced above).

Courts in analogous situations have found the quantity of testing to be adequate. For example, in In re Boller, 141 U.S.P.Q. 740 (C.C.P.A. 1964), the claimed invention was using volatile neutralizing agents in a chemical process. The patent specification described only a limited number of neutralizing agents that could be used in the process. The court, focusing on the claimed invention rather than on the absence of examples of other neutralizing agents that could be used in the process, held that the claim was broadly enabled:

> This is a broad invention and, as noted by the board, appellant is entitled to claims commensurate with the disclosure. Accordingly, we believe that appellant's disclosure, even though of a limited class of "volatile neutralizing agents," is sufficient to justify claims which define broadly a volatile neutralizing agent. Use of this term is commensurate with the breadth of the invention as disclosed. We think any chemist skilled in this art is fully apprised by appellant's disclosure of what the invention is and is taught how to use it. Appellant need not disclose every operative "volatile neutralizing agent."

Id. at 743 (citation omitted).

d. The state of the prior art

As evidenced by the lack of any prior art rejection, the prior art includes no suggestion that non-steroidal suppressors of angiogenesis can cause a reduction in hair growth. The invention thus is of pioneer status, and entitled to broad protection. As the court commented in In re Hogan, 194 U.S.P.Q. 527, 537 (C.C.P.A. 1977) (emphasis added):

> [W]e note appellants' argument that their invention is of "pioneer" status. The record reflects no citation of prior art disclosing a solid polymer of 4-methyl-1-pentene, which may suggest that appellants at least broke new ground in a broad sense. On remand, appellants may be found to have been in fact the first to conceive and reduce to practice "a solid polymer" as set forth in claim 13. As pioneers, if such they be, they would deserve broad claims to the broad concept.

e. The predictability of the art

The chemical/biochemical arts generally are unpredictable. This also applies to the state of the hair growth

art when applicants made their invention. Nobody knew that topical application of non-steroidal suppressors of angiogenesis actually would work until applicants conducted their research. But now that applicants have conducted their work, and established the broad applicability of their invention (see Table 1), it is predictable that non-steroidal suppressors of angiogenesis applied topically in an appropriate vehicle will work to reduce hair growth.

f. Breadth of the claims

Claim 1 covers no more than applicants' contribution -- the topical use of non-steroidal suppressors of angiogenesis to reduce hair growth.

2. The concerns of the Examiner

Applying the law to the present facts, applicants have enabled the claimed invention.

The Examiner's position regarding enablement appear to hinge largely on reference L, which says that mycophenolic acid (a species tested by applicants) can be used to increase hair growth. The Examiner begins by saying (p. 4 of action):

> As the cited reference [L] provided with this Office action discloses mycophenolic acid contrary to being a hair growth inhibitor is a hair growth stimulating compound and thus one of ordinary skill in the art could not practice the invention as claimed. The Examiner notes applicant's specification appears to be a shotgun specification for a whole slew of compounds and mycophenolic acid has not been disclosed or specifically singled out for inhibition of hair growth but appears to be only a "paper example" of an active which is contemplated or will be obtained at some future date experimental

> data showing mycophenolic acid as useful in inhibiting hair growth. However, prophetic test systems are not considered to provide any basis for presuming that the claimed method of treating using mycophenolic acid is enabled in mammalian subjects or human hosts. It is well known and established that "law requires that the disclosure in an application shall inform those skilled in the art how to use applicant's alleged discovery, not how to find out to use it for themselves." In re Gardner et al., 166 USPQ 138 (CCPA 1970).

But the Examiner got his facts wrong when he claims that mycophenolic acid is a "paper example." Applicants tested mycophenolic acid -- and 18 other examples -- according to the procedure described in the application in detail. As reported in Table 1, every compound (including mycophenolic acid) worked; each caused a significant reduction in hair growth. Moreover, applicants state in the application that the testing was conducted and, accordingly, the Examiner has no basis for calling the testing of the mycophenolic acid, and the testing of the other 18 compounds listed in Table 1, "paper" examples. But in any event, the enclosed Declaration of Dr. Ahluwalia (an inventor) verifies that the testing reported in Table 1 was in fact conducted.

Applicants further note that the 19 compounds that they tested are unrelated except for the fact that they are non-steroidal suppressors of angiogenesis. Thus, the disclosure in the specification in not a "shotgun" disclosure, but rather a disclosure of a large number of compounds linked by a common property.

The Examiner went on to discuss reference L in more detail:

> [T]he testing shown in the instant specification is very specific to certain conditions, certain vehicles, concentrations and mode or method of application. Please note that the reference disclosure teaches topical application of mycophenolic acid which is the same mode of application that applicants are disclosing for their mycophenolic acid. Please note that the reference L teaches that indeed this topical formulation when applied to the skin achieves the exact opposite result and furthermore it is noted that applicants have provided no guidance as to how the result can be achieved since the reference disclosure encompasses the entire claimed formulations as well as mode of application and concentration since applicants are respectfully directed to their very own instant specification which states the concentration of the compound can vary over a wide range. See page 8 last paragraph. The Examiner's position is that very broad disclosure which applicants assert is their contribution is actually encompassed by the prior art which shows the exact opposite result and thus one of ordinary skill in the art could not achieve the invention without undue experimentation in order to select optimum conditions, suitable vehicle, mode of application and concentration in order to achieve reduction in hair growth. Any angiogenesis would be inherent in the reference L whether it be promoting or inhibiting angiogenesis. Furthermore, it is not seen how applicants' **claimed invention** overcomes the promotion of hair growth achieved by the patent reference L.

As an initial matter, contrary to what the Examiner says, reference L is not prior art to the claimed invention. The "Publication Date" provided on reference L is May 2, 1995. The present application was filed prior to that date, on February 28,

1995. Thus, the claims in the present application do not have to "distinguish" reference L because reference L is not prior art.

Moreover, although reference L says that mycophenolic acid can be used to stimulate hair growth, applicants demonstrated through their testing that mycophenolic acid can be used for reducing hair growth. This testing includes not only experiments involving mycophenolic acid, but also experiments in which 18 other non-steroidal suppressors of angiogenesis were shown to reduce hair growth. Applicants thus have provided extensive evidence that non-steroidal suppressors of angiogenesis can be used to reduce hair growth, regardless of the teachings of reference L.

It is the duty of the Examiner who rejects a claim for lacking enablement to provide a reasonable support for the rejection, including why he questions any evidence of enablement provided by inventors. As the Court explained in In re Dinh-Nguyen, 181 U.S.P.Q. 46, 47 (C.C.P.A. 1974):

> Any assertion by the Patent Office that the enabling disclosure is not commensurate in scope with the protection sought must be supported by evidence or reasoning substantiating the doubts so expressed.

Similarly, in In re Marzocchi, 169 U.S.P.Q. 367, 370 (C.C.P.A. 1971), the court reasoned:

> [I]t is incumbent upon the Patent Office, whenever a rejection on this basis [lack of enablement] is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to

go to the trouble and expense of supporting his presumptively accurate disclosure.

The Examiner has pointed to reference L as a basis for contesting the accuracy of applicants' statements that mycophenolic acid can be used to reduce hair growth, but applicants already have provided substantial evidence in Table 1 that the statement is correct. Moreover, the Declaration of Dr. Ahluwalia submitted with this amendment provides verification that the testing actually was carried out. This is sufficient. Applicants are not required to conduct a further in-depth scientific investigation concerning reference L.

Conclusion

In view of the above, applicants submit that the claims are in condition for allowance, and such action is requested. Please charge any additional fees, or make any credits, to Deposit Account No. 06-1050.

Respectfully submitted,

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